REMARKS

The specification has been amended on page 4, line 2 to correct the recited ATCC Deposit No. for *Providencia sp.* PCM-1270 to read "3564". Both strains of *Providencia* are identified on page 4 with the same ATCC No., which is obviously a typographical error. The correct ATCC deposit number for *Providencia sp.* PCM 1270 is found on page 5, line 13, as well as the letter from the American Type Culture Collection dated August 3, 2001, which is attached to the accompanying declaration.

The specification has also been amended on page 5, line 16 to correct the date on which the designated bacteria strains were deposited with the ATCC, the correct date being found in the aforementioned letter of August 3, 2001 from the ATCC. Further, page 6 has been amended after line 12 to enter the full citation to Szwajcer et al, which citation is also found on page 18, lines 16-17 of the specification.

Claims 1-16 have been amended in accordance with the Examiner's suggestion found on page 4 of the communication of April 14, 2003, and to insert a phrase respecting the incubation time for producing 2-oxoglutaramate. Basis for such amendment can be found on page 7, lines 17-19 of the specification. Claim 6 has been amended to add the method for stopping incubation found on page 16, line 9 of the specification; namely, "disrupting the bacteria". Claim 16 has been amended by specifying that the bacteria or active catalyst has the capacity to convert (deaminate) L-glutamine to 2-oxoglutaramate, which disclosure is found on page 3, lines 8-9 of the specification.

Claims 31-40 are newly added and are drawn to the elected invention of claims 1-15. Hence, claims under active examination are 1-15 and 31-40.

Newly added claims 31-40 are directed to the method of claims 1-16 with the added provision that 2-oxoglutaramate product is separated from the incubation solution. Basis for claims 31-40 can be found in the original description and claims, e.g., pages 16,

17 and Example 4 of the description. No new matter has been added to the amended claims or to the newly added claims.

Rejection under 35 U.S.C. 103 (a)

Claims 1-15 have been rejected under 35 U.S.C. 103 (a) as being unpatenable over the article by Meister (Reference AS) taken with the article by Szwajcer et al (Reference AR). It is the Examiner's view that it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Meister by substituting bacterial cells or biocatalysts obtained from *Providencia* or *Proteus*, which are disclosed in Szwajcer et al, for the snake venom compositions disclosed by Meister. This rejection is respectfully traversed with respect to all of Applicant's pending claims.

As noted in the rejection, the primary reference, Meister, discloses the enzymatic oxidative deamination of Glutamine using snake venom in the presence of catalase. Also acknowledged in the rejection is that Meister does not disclose oxidative deamination of L-glutamine using bacterial cells or biocatalysts, much less such bacterial materials obtained from *Providencia* or *Proteus*, more particularly *Providencia* PCM 1270 and PCM 1298, or *Proteus mirabilis* PCM 1353. To supply this deficiency of the primary reference, the rejection relies upon the article by Szwajcer et al.

Szwajcer et al discloses the testing of certain bacteria, including those belonging to the genera *Proteus* and *Providencia*, (including *Proteus mirabilis* and *Providencia sp* PCM 1270 and PCM 1298) for their capacity to oxidize certain amino acids to their corresponding alpha-keto acids. Notably, L-glutamine was not tested.

The rejection states that "Szwajcer et al. disclose that at least *Providencia* PCM 1270 and PCM 1298 as well as *Proteus mirabilis* PCM 1353 are well known in the art to be suitable bacteria for the bioconversion of amino acids to the corresponding keto acid." This statement is too broad because the article by Szwajcer et al discloses only that such bacterial strains show L-amino acid oxidase activity for L-Methionine, and that *Providencia*

sp. PCM 1298 has amino acid oxidase activity for only some of the amino acids listed in Table 2 (page 411). Notably, L-glutamine is not included in the list found in Table 2

The rejection argues that L-tyrosine is structurally similar to L-glutamine, and that since Table 2 shows that *Providencia sp* PCM 1298 shows relative amino acid oxidase activity toward L-tyrosine, one of ordinary skill in the art would have expected similar activity toward L-glutamine. The underlying premise of this argument is not correct because L-tyrosine is not structurally similar to L-glutamine. L-tyrosine has a hydroxy substituted benzyl group at the terminal end of the molecule opposite the alpha amino acid group; whereas, L-glutamine has an amidoethyl group at the terminal end of the molecule opposite the alpha amino acid group. In fact, none of the amino acids listed in Table 2 of the Szwajcer et al article have an amido group at the terminal end of the amino acid molecule. L-tyrosine has an aromatic group (substituted with a hydroxyl group) at the terminal end of the molecule, while L-glutamine has no aromatic group in the molecule.

Like L-tyrosine, the amino acids Phenylalanine and Tryptophan have an aromatic group at their terminal ends. Table 2 of Szwajcer et al show that both of these amino acids also show relative activity with *Providencia sp* 1298. Other amino acids reported to have relative activity in Table 2 are those having a paraffinic group of from 3 to 4 carbon atoms in length (Methionine also having a sulfur group within the 3 carbon chain). These include Ethionine, Norvaline, Leucine and Norieucine. However, other amino acids having such a paraffinic group did not show any relative activity; namely, alanine, valine, and isoleucine. Consequently, the presence of a paraffinic group of 3 to 4 carbons at the terminal end of the amino acid molecule opposite the amino acid group cannot be a predictor of activity for conversion to the corresponding keto acid using *Providencia sp* 1298 based on the record at hand.

Nor is the presence of a polar group on the terminal end of the amino acid molecule a predictor of relative activity. Note that Serine, Threonine, Lysine and Aspartic acid all have

polar groups at the terminal end of the molecule and these amino acids showed no relative activity.

Szwajcer et al, therefore, provides no predictable pattern from which one skilled in the art can draw any conclusions as to whether any particular amino acid would be converted to its corresponding alpha keto acid using *Providencia sp* 1298. One skilled in the art would be required to test each amino acid individually.

More specifically, one skilled in the art would not conclude from the references at hand that L-glutamine would be converted to its corresponding alpha keto acid using *Providencia sp* 1298 for the reasons that (1) L-glutamine was not tested by Szwajcer et al. (2) L-glutamine is not structurally similar to L-tyrosine, and (3) the disclosure of Szwajcer et al does not provide one skilled in the art sufficient information from which a predictable pattern of L-amino acid oxidase activity to *Providencia sp* 1298 can be derived. Hence, the Examiner's conclusion respecting the obviousness of the claimed invention is not supported by an appropriate analysis under 35 U.S.C. 103.

It is now established jurisprudence that where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under 35 U.S.C. 103 requires, inter alia, consideration of two factors; namely, (1) whether the prior art would have suggested to those of ordiary skill in the art that they should make the claimed composition or device, or carry out the claimed process, and (2) whether the prior art could also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

The obviousness rejection is deficient since the Examiner has only considered one factor, i.e., the reasonable expectation of success. The Examiner has derived the first factor of motivation/suggestion from the second factor of reasonable expectation of success. The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733

F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). A teaching or motivation to combine prior art references must be clear and particular. In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999).

On the record at hand, the Examiner has not established a prima facie case of obviousness. Reconsideration of the rejection under 35 U.S.C. 103 is respectfully requested.

Rejections under 35 U.S.C. 112

Claims 4 and 12 have been rejected under the first paragraph of 35 U.S.C 112. The rejection argues that it is not clear that the deposit of bacteria with the American Type Culture Collection (ATCC) noted on page 5 of the specification meets all of the criteria prescribed in 37 CFR 1.801 to 1.809. This rejection is respectfully traversed. The criteria prescribed in sections 1.801 to 1.809 of 37 CFR as to permanence of deposit, accessibility thereto by the public or to the Commissioner of Patents, restrictions as to availability, term of maintenance and identification by accession number are all standard criteria of deposits of this type made with the ATCC.

Accompanying this amendment is a declaration by the undersigned attorney (as suggested in the rejection) that avers that the five requirements stated in items 2-6 on page 3 of the office action have been met, which thereby satisfies the criteria set forth in the aforestated sections of 37 CFR. Accordingly, since the deposits are referred to in the body of the specification, are identified by their deposit (accession) numbers, the date of deposit and the name and address of the depository, and in view of the averments in the accompanying declaration, it is submitted that the foregoing submissions are fully responsive to this rejection under 35 U.S.C. 112. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-13 have been rejected as indefinite under the second paragraph of 35 U.S.C. 112 because the claims are incomplete in the absence of the recitation of a recovery step for the 2-oxoglutaramate product. It is argued in the rejection that it would be expected

from conventional preparation processes that the 2-oxoglutaramate product must be isolated or recovered. This rejection is respectfully traversed.

2-oxoglutaramate is useful as a plant growth regulator (page 1, lines 14-15 of the specification). The reaction mixture produced by the claimed method can be used as-is or with the bacteria killed or disrupted, with nothing further done to purify and/or concentrate the 2-oxoglutaramate product (page 16, lines 7-10 of the specification). Thus the reaction mixture can be applied to plants as is and does not require isolation, recovery or purification of the 2-oxoglutaramate product, although such steps are contemplated and described in the specification. Claims 1-13 are therefore not indefinite and fully comply with the requirements of 35 U.S.C. 112 (second paragraph). Hence, this rejection is not appropriate, as applied to the facts of the invention described in the specification. Reconsideration and withdrawal of this rejection is respectfully requested.

Newly presented claims 31 to 40 have been submitted to include a recovery step for a material comprising 2-oxoglutaramate from the incubation solution in the event that the Examiner continues to maintain the foregoing rejection under 35 U.S.C. 112 (second paragraph).

It is further asserted in the rejection (page 4) that claim 1 is confusing in the recitation of "a biocatalyst derived therefrom". It is suggested in the rejection that the term "obtained from" would be remedial. The claims have been amended to adopt this suggestion. This amendment is made only for clarification. The amendment does not alter the scope of the claims or surrender any subject matter. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

The Restriction Requirement

Applicant's argument traversing the restriction requirement was not found persuasive by the Examiner because Applicant has not demonstrated with objective evidence that the composition, as claimed, cannot be used to produce other products, such as single cell

protein for nutritional supplementation or other enzymatic products. Reconsideration is respectfully requested in view of the following remarks.

Section 806.05(h) of the Manual of Patent Examining Procedure (MPEP) states that a product and a process of using the product are only shown to be distinct inventions if either (A) the process of using, *as claimed*, can be practiced with another materially different product, or (B) the product, *as claimed*, can be used in a materially different process. It is submitted that the Examiner has not given appropriate weight to the term "*as claimed*" in that section of the MPEP.

It is clear (and the rejection does not dispute) that the process of using (claims 1-16 and 31-40) cannot be practiced with another materially different product since these claims definitively specify the product (2-oxoglutaramate), the bacteria (*Providencia and Proteus*) used and the starting material (L-glutamine). With respect to the reaction mixture (claims 16 –26), these claims are directed to a "reaction mixture for producing 2-oxoglutaramate" comprising the same bacteria and starting material that are specified in the process claims. Therefore, *as claimed*, the reaction mixture produces 2-oxoglutaramate and not other products, such as single cell proteins for nutritional supplementation or other enzymatic products. The instant proposed amendment to claim 16 amends claims 16-26 by further specifying that the designated bacteria or active biocatalyst have the capacity to convert L-glutamine to 2-oxoglutaramate, thereby further making clear that the reaction mixture produces 2-oxoglutaramate.

A thorough search of the prior art for the method of claims 1-15 should also include a search of the art encompassing the reaction mixture of claims 16-26, which reaction mixture includes the same starting material and the same bacteria as found in the method claims. Hence a search of claims 1-15 is coextensive with a search of claims 16-26. To restrict these two groups of claims places a burden (financial and otherwise) on both the Applicant and the Patent Office since the subject matter of both sets of claims can be handled simultaneously. Moreover, the public is not served by multiplying the number of granted

patents that cover related, but non-distinct, subject matter. Reconsideration and withdrawal of the restriction requirement are respectfully requested.

In the event that the Examiner considers any matter raised in the communication of April 14, 2003 to be still unresolved, the Examiner is invited to phone Applicant's representative at the number indicated below in order to expedite the resolution of any such matter.

Respectfully submitted,

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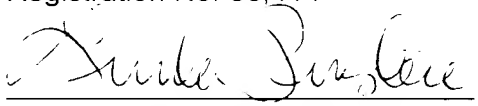

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Please amend the specification as follows:

Amend the paragraph bridging pages 3 and 4 to read as follows.

The method for producing 2-oxoglutaramate includes incubating Providencia or Proteus bacteria or an active biocatalyst ~~derived therefrom~~obtained from such bacteria in an incubation solution comprising at least about 25mM (millimolar) of L-glutamine. Specific Providencia and Proteus strains include, without limitation, Providencia sp. PCM-1298, ATCC Deposit No. PTA-3563, Providencia sp. PCM-1270, ATCC Deposit No PTA-~~3563~~3564, and Proteus mirabilis PCM-1353, ATCC Deposit No. PTA-3562. The L-glutamine typically is added to the incubation solution prior to addition of the bacteria. Additionally, or alternatively, L-glutamine may be added to a culture already containing bacteria. The L-glutamine may be added as a single aliquot, or continuously over a period of time, for continuous-feed processes, either in two or more aliquots or as a steady trickle. The incubation solution may be an aqueous slurry comprising solid L-glutamine.

Amend page 5, lines 6-21 to read as follows:

Described herein is a method for producing 2-oxoglutaramate, a chemical compound with value as a plant growth regulator. Current manufacturing methods for producing 2-oxoglutaramate are not commercially practicable. The method of the present invention is a process by which L-glutamine is incubated in the presence of bacteria of the Providencia genus, such as Providencia sp., and including Providencia strains PCM-1270, ATCC Deposit No. PTA-3564, and PCM-1298, ATCC Deposit No. PTA-3563, and/or bacteria of the Proteus genus, for instance Proteus mirabilis, such as strain PCM-1353, ATCC Deposit No. PTA-3562, each of which were deposited on ~~August 23~~July 25, 2001 at the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, U.S.A. The designation "PCM-XXXX" refers to accession numbers of the Polish Collection of Microorganisms, Institute of Immunology and Experimental Therapy, Wroclaw, Poland.

Please amend page 6, lines 12-16 to read as follows:

(II) Szwajcer E. et al. Providencia medium

(Enzyme Microbiol. Tech., 1982, Vol. 4, pp 409-413)

10g/L bactopeptone

2g/L casein hydrolysate

2g/L yeast extract

6g/L NaCl or 10mm CaCl2

Please amend the claims to read as follows:

1. (currently amended) A method for producing 2-oxoglutaramate, comprising the step of incubating bacteria of the genera Providencia or Proteus, or an active biocatalyst ~~derived therefrom~~obtained from either of said bacteria, in an incubation solution comprising at least about 25mM L-glutamine for a time sufficient to produce a product comprising 2-oxoglutamarate.

2. (original) The method of claim 1, in which the incubation solution comprises at least about 100mM L-glutamine.

3. (original) The method of claim 1, in which the incubation solution comprises a buffer and catalase and has a pH ranging from 6.5 to 8.5.

4. (currently amended) The method of claim 1, in which the bacteria ~~are one of~~is Providencia sp. PCM-1298 ~~and~~ or Providencia sp. PCM-1270.

5. (original) The method of claim 1, in which L-glutamine is added to the incubation solution during incubation over a time period either in two or more aliquots or as a steady trickle.

6. (currently amended) The method of claim 1, further comprising the step of stopping the incubation by either killing the bacteria, disrupting the bacteria or removing the bacteria from the incubation solution.

7. (currently amended) The method of claim 1, further comprising the step of purifying the 2-oxoglutaramate product by ion exchange chromatography.

8. (currently amended) The method of claim 1, further comprising the step of purifying the 2-oxoglutaramate product by precipitation.

9. (original) The method of claim 1, in which the incubation solution is a slurry comprising solid L-glutamine.

10. (original) The method of claim 9, in which the slurry comprises up to about 250 g/L of solid L-glutamine.

11. (currently amended) The method of claim 1, in which the bacteria is Proteus mirabilis.

12. (currently amended) The method of claim 11, in which the bacteria is Proteus mirabilis strain PCM-1353.

13. (currently amended) The method of claim 1, in which the active biocatalyst is immobilized on a substrate

14. (currently amended). A method for producing 2-oxoglutaramate, comprising the steps of:

a) providing an incubation solution slurry comprising a buffer and solid L-glutamine, said solution slurry ~~and~~ having a pH of from about 7.0 to about 8.0;

b) adding to the incubation solution slurry a resuspended wet cell pellet ~~collected from one~~ of a Providencia culture ~~and~~ or a Proteus culture; and

c) incubating the slurry to convert L-glutamine to 2-~~oxoglutaramic acid~~oxoglutaramate.

15. (original) The method of claim 14, in which the slurry further comprises catalase.

16. (currently amended) A reaction mixture for producing 2-oxoglutaramate, comprising *Providencia* or *Proteus* bacteria or an active biocatalyst ~~derived therefrom~~obtained from either of said bacteria, and at least about 25 mM L-glutamine, said bacteria or active biocatalyst having the capacity to convert L-glutamine to 2-oxoglutaramate.

17. (currently amended) The reaction mixture of claim 16, in which the bacteria ~~are~~ is ~~one of~~ *Providencia sp.* PCM-1298 ~~and~~ or *Providencia* sp. PCM-1270.

18. (currently amended) The reaction mixture of claim 16, in which the bacteria is *Proteus mirabilis*.

19. (currently amended) The reaction mixture of claim 18, in which the bacteria is *Proteus mirabilis* strain PCM-1353.

20. (original) The reaction mixture of claim 16, comprising a near-saturation amount of L-glutamine.

21. (original) The reaction mixture of claim 16, comprising a slurry of solid L-glutamine.

22. (currently amended) The reaction mixture of claim 21, in which the slurry comprises up to about 250g/L of solid L-glutamine.

23. (original) The reaction mixture of claim 16, further comprising catalase.

24 (currently amended) The reaction mixture of claim 16, comprising an active biocatalyst ~~derived~~ obtained from *Providencia* or *Proteus* bacteria that is immobilized on a substrate.

25. (original) The reaction mixture of claim 16, comprising at least about 1% w/v, wet cell pellet mass, of the bacteria cells.

26. (original) The reaction mixture of claim 21, comprising from 1% by weight to 50% by weight bacteria (wet cell pellet mass), 50mM TRIS-HCl (pH 7.0 to 8.0), catalase and from 0.32% by weight to 25% by weight L-glutamine.

27 (original) A composition comprising *Providencia* or *Proteus* bacteria and at least about 20mM 2-oxoglutaramate.

28 (currently amended) The composition of claim 27, in which the bacteria ~~are one of~~ is *Providencia sp.* PCM-1298, ~~and~~ or *Providencia sp.* PCM-1270.

29 (currently amended) The composition of claim 27, in which the bacteria is *Proteus mirabilis*.

30. (currently amended) The composition of claim 29, in which the bacteria is *Proteus mirabilis* strain PCM-1353.

31. (new) A method for producing 2-oxoglutaramate, comprising the steps of (a) incubating bacteria of the genera *Providencia* or *Proteus*, or an active biocatalyst obtained from either of said bacteria, in an incubation solution comprising at least about 25mM of L-glutamine for a time sufficient to produce a product comprising 2-

oxoglutaramate, and (b) separating a material comprising 2-oxoglutaramate from said incubation solution.

32 (new) The method of claim 31 wherein the bacteria is *Providencia sp.* PCM-1298, *Providencia sp.* PCM-1270, or *Proteus mirabilis* PCM-1353.

33 (new) The method of claim 32 wherein the incubation solution has a pH of from about 6.5 to about 8.5.

34 (new) The method of claim 33 wherein the period of incubation is from about 1 to about 24 hours.

35 (new) The method of claim 32 wherein the incubation solution comprises at least about 250mM of L-glutamine.

36. (new) The method of claim 33 wherein the concentration of L-glutamine in the incubation solution is near saturation.

37. (new) The method of claim 32 further comprising purifying 2-oxoglutaramate separated from the incubation solution.

38 (new) The method of claim 33 wherein the incubation solution comprises a buffer and has a pH of from about 7 to about 8.

39. (new) The method of claim 31 wherein step (b) comprises stopping the incubation by either killing the bacteria, disrupting the bacteria, or removing the bacteria from the incubation solution.

40. (new) The method of claim 39 further comprising the step of purifying 2-oxoglutaramate product by ion exchange chromatography.